REMARKS

Claims 8-10 and 17-29 are currently pending in the application. Applicants acknowledge the Examiner's indication that claims 19, 23 and 29 are merely objected to.

Rejection of claims 8-10, 17, 18, 20-22 and 24-28 under 35 U.S.C. § 112, first paragraph

Claims 8-10, 17, 18, 20-22 and 24-28 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner indicates that "the specification does not describe a genus of variants for amino acids sequences at least 90% identical to the amino acid sequence of residues 50-197 of SEQ ID NO: 4, or SEQ ID NO: 4 or 5 for the claimed method... and there is no disclosure of any particular structure to function/activity relationship in the disclosed species." Applicants respectfully traverse this rejection.

The application, and in particular the Examples, provides extensive information regarding structure to function/activity relationship of Csp1 (SEQ ID NO: 4) and that of a fragment of amino acids 50-197 of SEQ ID NO: 4. For example, Figure 5 shows the domains in Csp1 that are involved in calcineurin binding and inhibition (see the figure legend at page 8, lines 9-19, as well as the text at page 127, lines -26). In particular, Figures 5 A and B show that Csp1 lacking the N-terminus (Csp1 50-197; 101-197; and 150-197) is sufficient to inhibit the nuclear import of NF-AT4 stimulated by calcium ionophore. The figure further shows that Csp1 lacking the C-terminal half (Csp 1-50 and 1-100) fails to block calcium activation of NF-AT4 nuclear import. Furthermore, the specification describes that Csp1 comprises a sequence element (ERMRRP), which is located in the C-terminal half of the protein, and which appears to be similar to the consensus autoinhibitory domain of mammalian calcineurin (page 127, lines 15-19). The specification further describes that separate mutations affecting the ERM, RRPE or other conserved sequence elements such as LIS108, did not prevent Csp1's inhibition of calcineuin-dependent translocation of NF-AT to the nucleus, nor Csp1 binding to calcineurin in vitro (page 127, lines 20-22). However, Csp1 with a mutation in the RRPE sequence was defective in its ability to block hydrolysis of small substrates, e.g., pNPP, by calcineurin (page 127, lines 22-26, and page 131, lines 24-25 and Fig. 15). Thus, the specification provides extensive structure to function/activity description.

Regarding Csp2 (SEQ ID NO: 5), the specification describes that Csp2 lacks the ERM sequence, but shares considerable homology with Csp1 in a sequence block that is highly conserved in the Csps and contains basic residues (PKPKIIQTRRPE) (page 127, lines 17-19).

Thus, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Applicants believe that no fees are due in association with this submission. However, if any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to Deposit Account Number **06-1448, Reference HMV-048.01**.

Respectfully submitted,

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